

Remarks

Applicants respectfully note that an amendment of the Title of the instant application was submitted in a Preliminary Amendment filed by Applicants on November 6, 2000, a copy of which is attached hereto as Exhibit A.

Applicants further respectfully note that amendment of the priority information contained in the first paragraph of the instant application to replace the blank line and Attorney Docket number with U.S. Provisional Application No. 60/147,823, was also submitted in the Preliminary Amendment filed by Applicants on November 6, 2000 (see Exhibit A). Applicants have also corrected the typographical error within the priority filing date of U.S. Provisional Application No. 60/147,823.

The language of the cross-reference to related applications has been further amended such that the language conforms to the guidelines as presently set forth, and thus, no new matter has been added.

Claims 48-56, 86-87, 89 sub-parts (b)-(f) and 90-95 have been canceled herein. Claims 1-23, 38-45, 57-58, 60-85, and 88 were canceled previously. No new matter has been added by the amendments to the claims. Claims 24-37, 46-47, 59, and 89 will be pending after entry of this amendment.

Formal Matters

Correction of Inventorship

Applicants respectfully note that an amendment to delete inventors Luisa Iruela-Arispe and Steven M. Ruben was included in the Preliminary Amendment filed on November 6, 2000 (see Exhibit A).

Applicants further respectfully note that a Petition Under 37 C.F.R. § 1.48(b)(1) to Correct Inventorship in a Nonprovisional Patent Application, along with the applicable petition fee, was also filed by Applicants on November 6, 2000. A copy of the Petition is attached as Exhibit B. Specifically, Applicants petitioned to delete Luisa Iruela-Arispe and Steven M. Ruben from the inventive entity as those persons' contributions were no longer claimed as a result of amendment or cancellation of claims during prosecution of the instant application.

Request for Corrected Filing Receipt

Applicants respectfully note that a Request for Corrected Filing Receipt requesting deletion of inventors Luisa Iruela-Arispe and Steven M. Ruben, as well as correction of the spelling of the name of inventor Zdenka L. Jonak, was submitted on October 21, 2001. The subsequent "Corrected" Filing Receipts mailed September 25, 2002 and May 15, 2003 failed to include the requested corrections. Applicants therefore submit concurrently herewith a Second Request for Corrected Filing Receipt which requests (a) deletion of Luisa Iruela-Arispe and Steven M. Ruben from the inventive entity; (b) correction of the spelling of the names of inventors Zdenka L. Jonak and Jonathan A. Terrett; and (c) inclusion of priority U.S. Provisional Application No. 60/147,823.

Information Disclosure Statements

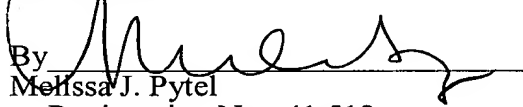
Applicants respectfully note that the Information Disclosure Statements, along with Forms 1449, filed by Applicants on September 15, 1999 and May 10, 2000, were not initialed and returned by the Examiner by the date of the mailing of the Notice of Allowance. Therefore, Applicants respectfully request that the Examiner indicate consideration of the references by initialing and returning a copy of the submissions to Applicants at her earliest convenience. Copies of the Information Disclosure Statements, with Forms 1449, are attached hereto as Exhibits C and D, respectively.

Conclusion

Applicants respectfully request that aforementioned amendments and remarks be entered and made of record in the file history of the instant application prior to issuance as a United States Patent. If there are any fees due in connection with the filing of this paper, please charge the fees to our Deposit Account No. 08-3425. If a fee is required for an extension of time under 37 C.F.R. § 1.136, such an extension is requested and the fee should also be charged to our Deposit Account.

Dated: September 30, 2005

Respectfully submitted,

By 
Melissa J. Pytel

Registration No.: 41,512
HUMAN GENOME SCIENCES, INC.
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MMW/MJP/ba



Exhibit A

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Iruela-Arispe *et al.*

Appl. No. 09/373,658

Filed: August 13, 1999

For: **Meth1 Polynucleotides** (as amended)

Art Unit: 1642

Examiner: Johnson, N.

Atty. Docket: 1488.1070006

Preliminary Amendment

Commissioner for Patents
Washington, D.C. 20231

Sir:

In advance of prosecution, please amend the application as follows.

In the Inventorship

In the inventorship, please delete "Luisa Iruela-Arispe" and "Steven M. Ruben."

In the Title

Please delete the existing title and insert therefor --Meth1 Polynucleotides--.

In the Specification

At page 1, line 11, please delete "_____" (Attorney Docket No. 1488.1070005)", and insert therein --60/147,823--.

At page 102, lines 27-28, please delete "SEQ ID NO:125" and insert therein --SEQ ID NO:126, encoded by SEQ ID NO:125,--.

At page 153, line 17, please delete "SEQ ID NO:125" and insert therein --SEQ ID NO:126--.

Please cancel the existing Sequence Listing for the above-identified application, replace it with the substitute Sequence Listing appended hereto, and insert the same at the end of the application.

In the Claims

Please cancel claims 1-23 without prejudice to or disclaimer of the subject matter therein. Please add the following new claims.

-- 24. An isolated polynucleotide comprising a nucleotide sequence encoding amino acids 1 to 967 of SEQ ID NO:126.

25. The isolated polynucleotide of claim 24, wherein said polynucleotide comprises nucleotides 466 to 3366 of SEQ ID NO:125.

26. The isolated polynucleotide of claim 24, wherein said nucleotide sequence comprises the entire nucleotide sequence of SEQ ID NO:125.

27. The isolated polynucleotide of claim 24, which is RNA.

28. The isolated polynucleotide of claim 25, which is RNA.

29. The isolated polynucleotide of claim 26, which is RNA.

30. The isolated polynucleotide of claim 24, which is DNA.
31. The isolated polynucleotide of claim 25, which is DNA.
32. The isolated polynucleotide of claim 26, which is DNA.
33. A vector comprising the isolated polynucleotide of claim 24.
34. The vector of claim 33, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.
35. A host cell which comprises the isolated polynucleotide of claim 24.
36. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 33.
37. A process for producing a polypeptide comprising culturing the host cell of claim 36 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.
38. An isolated polynucleotide which hybridizes at 42°C in 50% formamide, 5xSSC, 50 mM sodium phosphate, 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured,

sheared salmon sperm DNA, followed by washing in 0.1xSSC at 65°C, with a probe consisting of nucleotides 466 to 3366 of SEQ ID NO:125.

39. The isolated polynucleotide of claim 38, which is RNA.
40. The isolated polynucleotide of claim 38, which is DNA.
41. A vector comprising the isolated polynucleotide of claim 38.
42. The vector of claim 41, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.
43. A host cell which comprises the isolated polynucleotide of claim 38.
44. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 41.
45. A process for producing a polypeptide comprising culturing the host cell of claim 43 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.
46. An isolated polynucleotide comprising a nucleotide sequence which is complementary to a polynucleotide sequence encoding amino acids 1 to 967 of SEQ ID NO:126.

47. The isolated polynucleotide of claim 46, comprising a nucleotide sequence which is complementary to nucleotides of 466 to 3366 SEQ ID NO:125.

48. An isolated polynucleotide comprising a nucleotide sequence at least 95% identical to the nucleotide sequence of SEQ ID NO:125.

49. The isolated polynucleotide of claim 48, comprising a nucleotide sequence at least 95% identical to nucleotides 466 to 3366 of SEQ ID NO:125.

50. The isolated polynucleotide of claim 49, which is RNA.

51. The isolated polynucleotide of claim 49, which is DNA.

52. A vector comprising the isolated polynucleotide of claim 49.

53. The vector of claim 52, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.

54. A host cell which comprises the isolated polynucleotide of claim 49.

55. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 52.

56. A process for producing a polypeptide comprising culturing the host cell of claim 54 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.

57. An isolated polynucleotide comprising a nucleotide sequence encoding amino acids 1 to 950 of SEQ ID NO:2.

58. The isolated polynucleotide of claim 57, comprising nucleotides 1 to 2853 of SEQ ID NO:1.

59. The isolated polynucleotide of claim 58, comprising the entire nucleotide sequence of SEQ ID NO:1.

60. The isolated polynucleotide of claim 57, which is RNA.

61. The isolated polynucleotide of claim 57, which is DNA.

62. A vector comprising the isolated polynucleotide of claim 57.

63. The vector of claim 62, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.

64. A host cell which comprises the isolated polynucleotide of claim 57.

65. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 62.

66. A process for producing a polypeptide comprising culturing the host cell of claim 64 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.

67. An isolated polynucleotide comprising a nucleotide sequence which is complementary to a polynucleotide sequence encoding amino acids 1 to 950 of SEQ ID NO:2.

68. The isolated polynucleotide of claim 67, comprising a nucleotide sequence which is complementary to nucleotides 1 to 2853 of SEQ ID NO:1.

69. An isolated polynucleotide which hybridizes at 42°C in 50% formamide, 5xSSC, 50 mM sodium phosphate, 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA, followed by washing in 0.1xSSC at 65°C, with a probe consisting of nucleotides 1 to 2853 of SEQ ID NO:1.

70. The isolated polynucleotide of claim 69, which is RNA.

71. The isolated polynucleotide of claim 69, which is DNA.

72. A vector comprising the isolated polynucleotide of claim 69.

73. The vector of claim 72, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.

74. A host cell which comprises the isolated polynucleotide of claim 69.

75. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 73.

76. A process for producing a polypeptide comprising culturing the host cell of claim 74 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.

77. An isolated polynucleotide comprising a nucleotide sequence at least 95% identical to the nucleotide sequence of SEQ ID NO:1.

78. The isolated polynucleotide of claim 77, comprising a nucleotide sequence at least 95% identical to nucleotides 1 to 2853 of SEQ ID NO:1.

79. The isolated polynucleotide of claim 78, which is RNA.

80. The isolated polynucleotide of claim 78, which is DNA.

81. A vector comprising the isolated polynucleotide of claim 78.

82. The vector of claim 81, wherein said polynucleotide is operably associated with a regulatory sequence that regulates gene expression.

83. A host cell which comprises the isolated polynucleotide of claim 78.

84. A process for producing a host cell comprising transforming or transfecting a cell with the vector of claim 81.

85. A process for producing a polypeptide comprising culturing the host cell of claim 83 under conditions sufficient for the production of said polypeptide and recovering said polypeptide from the culture.--

Remarks

Support for the claims can be found throughout the specification. The specification has been amended to insert priority information, to correct SEQ ID NO:s, and to insert a new sequence listing. The sequence listing differs in the addition of SEQ ID NO:125. SEQ ID NO:125 is identical to SEQ ID NO:1 of priority Appl. No. 08/845,496. Appl. No. 08/845,496 was incorporated by reference in its entirety in the captioned application. Thus, the addition of SEQ ID NO:125 in the substitute sequence listing does not constitute new matter. SEQ ID NO:125 from the original sequence listing is represented as SEQ ID NO:126 in the substitute sequence listing.

In accordance with 37 C.F.R. § 1.825(b), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith are the same.

It is respectfully believed that this application is now in condition for examination. Early notice to this effect is respectfully requested

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Andrea Jo Kamage

Andrea Jo Kamage
Agent for Applicants
Registration No. 43,703

Date: November 6, 2000

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Washington, D.C. 20005-3934
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Exhibit B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Iruela-Arispe *et al.*

Appl. No. 09/373,658

Filed: August 13, 1999

For: **Meth1 Polynucleotides** (as amended)

Art Unit: 1642

Examiner: Johnson, N.

Atty. Docket: 1488.1070006

**Petition Under 37 C.F.R. § 1.48(b)(1) To Correct
Inventorship In A Nonprovisional Patent Application**

Commissioner for Patents
Washington, D.C. 20231

Sir:

Applicants petition to correct inventorship in the above-captioned nonprovisional patent application. Prosecution of the application has resulted in the amendment or cancellation of claims so that fewer than all of the currently named inventors are the actual inventors of the invention being claimed in the application. Specifically, Applicants petition to delete Luisa Iruela-Arispe and Steven M. Ruben from the inventive entity as those persons' contributions are no longer claimed in the application. Accordingly, upon granting of this petition, the inventive entity would be changed from "Luisa Iruela-Arispe, Gregg A. Hastings, Steven M. Ruben, Zdenka L. Jorak, Stephen H. Trulli, James A. Fronwald and Jonathan A. Terret" to --Gregg A. Hastings, Zdenka L. Jorak, Stephen H. Trulli, James A. Fronwald and Jonathan A. Terret--.

This petition is accompanied by:

- (1) An amendment directing the cancellation of Luisa Iruela-Arispe and Steven M. Ruben from the inventive entity;
and

- (2) The petition fee as set forth under 37 C.F.R. § 1.17(i), in
our attached check no. 29377 for 130.00.

Applicants hereby authorize the U.S. Patent and Trademark Office to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036. A duplicate copy of this petition is enclosed.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Andrea Jo Kamage

Andrea Jo Kamage
Agent for Applicants
Registration No. 43,703

Date: November 6, 2000

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Suite 600
Washington, D.C. 20005-3934
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Exhibit C

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

IRUELA-ARISPE *et al.*

Appl. No. 09/373,658

Filed: August 13, 1999

For: **Meth1 and Meth2 Polynucleotides
and Polypeptides**

Art Unit: To be assigned

Examiner: To be assigned

Atty. Docket: 1488.1070006/EKS/AJK

Information Disclosure Statement

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. Copies of documents AM1, AN1 and AR21 are submitted herewith. Copies of the remaining documents were cited by or submitted to the Office in Application No. 09/235,810, filed January 22, 1999, which is relied upon for an earlier filing date under 35 U.S.C. § 120. Thus, copies of those documents are not attached. 37 C.F.R. § 1.98(d).

Document AM1, WO 98/55643, is in a foreign language. An English language translation of Document AM1 is provided as Document AR21.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the

undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

The Examiner's attention is directed to co-pending U.S. Patent Application Nos. 09/235,810, filed January 22, 1999 and 09/318,208, filed May 25, 1999, which are directed to related technical subject matter.

Applicants wish to bring to the attention of the Examiner that SEQ ID NO:1 and the corresponding clone of this application may be considered to be related to the following SEQ ID NOs, in the following co-pending applications:

SEQ ID NOs	U.S. Appl. No.	Filing Date
1220	08/103,744	August 9, 1993
5625	08/104,507	August 9, 1993
6424	08/196,363	February 15, 1994
3446 and 4403	08/803,609	February 21, 1997
1787	09/076,898	May 13, 1998

Applicants also wish to bring to the attention of the Examiner that SEQ ID NO:3 and the corresponding clone of this application may be considered to be related to the following SEQ ID NOs, in the following co-pending applications:

SEQ ID NOs	U.S. Appl. No.	Filing Date
1219	08/103,744	August 9, 1993
1172	08/104,507	August 9, 1993
2771 and 16001	08/196,363	February 15, 1994
3785	08/196,362	February 15, 1994
1214	08/220,661	March 31, 1994
1370	08/220,691	March 31, 1994

SEQ ID NOs	U.S. Appl. No.	Filing Date
1665	08/276,163	July 15, 1994
5785	08/346,731	November 21, 1994
2002	08/803,610	February 21, 1997
5063	08/971,050	November 14, 1997
6602 and 11925	08/971,197	November 14, 1997
1219, 4278 and 4296	08/976,343	November 21, 1997
710 and 752	08/985,366	November 4, 1997
3482	08/985,356	December 4, 1997
1360	09/078,614	May 14, 1998

The identification of these U.S. Patent Applications is not to be construed as a waiver of secrecy as to those applications now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited applications and the art cited therein during examination.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

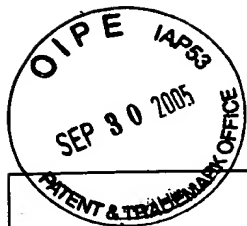
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Andrea Jo Kamage
Agent for Applicants
Registration No. 43,703

Date: September 15, 1994

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FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1488.1070006APPLICATION NO.
09/373,658APPLICANT
Iruela-Arispe *et al.*FILING DATE
August 13, 1999GROUP
To be assigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	EP 0 874 050 A2	10/28/1998	Europe			Yes No
	AM1	WO 98/55643	12/10/1998	WIPO			Yes No
	AN1	WO 99/07850	02/18/1999	WIPO			Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	1	Adams, J.C., "Molecules in Focus: Thrombospondin-1," <i>Int. J. Biochem. Cell Biol.</i> 29:861-865 (June 1997)
AS	1	Asch, A.S. <i>et al.</i> , "Analysis of CD36 Binding Domains: Ligand Specificity Controlled by Dephosphorylation of an Ectodomain," <i>Science</i> 262:1436-1440 (1993)
AT	1	Bjarnason, J.B. and J.W. Fox, "Snake Venom Metalloendopeptidases: Reprolysins," <i>Meth. Enzymol.</i> 248:345-369 (1995)

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



FORM PTO-1449 <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 1488.1070006	APPLICATION NO. 09/373,658
	APPLICANT Iruela-Arispe <i>et al.</i>	
	FILING DATE August 13, 1999	GROUP To be assigned

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	AA						
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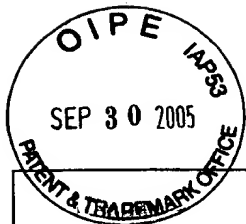
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>2</u>	Bornstein, P., "Thrombospondins: structure and regulation of expression," <i>FASEB J.</i> 6:3290-3299 (1992)
	AS	<u>2</u>	Catimel, B. <i>et al.</i> , "Human platelet glycoprotein IIb binds to thrombospondin fragments bearing the C-terminal region, and/or the type I repeats (CSVTCG motif), but not to the N-terminal heparin-binding region," <i>Biochem. J.</i> 284:231-236 (1992)
	AT	<u>2</u>	Colige, A. <i>et al.</i> , "cDNA cloning and expression of bovine procollagen I N-proteinase: A new member of the superfamily of zinc-metalloproteinases with binding sites for cells and other matrix components," <i>Proc. Natl. Acad. Sci. USA</i> 94:2374-2379 (March 1997)

EXAMINER	DATE CONSIDERED
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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>3</u>	Dameron, K.M. <i>et al.</i> , "Control of Angiogenesis in Fibroblasts by p53 Regulation of Thrombospondin-1," <i>Science</i> 265:1582-1584 (1994)
	AS	<u>3</u>	Dawson, D.W. <i>et al.</i> , "CD36 Mediates the In Vitro Inhibitory Effects of Thrombospondin-1 on Endothelial Cells," <i>J. Cell Biol.</i> 138:707-717 (August 1997)
	AT	<u>3</u>	Guo, N.-H. <i>et al.</i> , "Heparin-binding Peptides from the Type I Repeats of Thrombospondin," <i>J. Biol. Chem.</i> 267:19349-19355 (1992)

EXAMINER

DATE CONSIDERED

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INFORMATION DISCLOSURE STATEMENT

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	AM						Yes No
	AN						Yes No
	AO						Yes No
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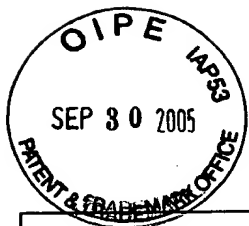
OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>4</u>	Guo, N.-H. <i>et al.</i> , "Antiproliferative and antitumor activities of D-reverse peptides derived from the second type-1 repeat of thrombospondin-1," <i>J. Peptide Res.</i> 50:210-221 (September 1997)
	AS	<u>4</u>	Iruela-Arispe, M.L. <i>et al.</i> , "Differential Expression of Thrombospondin 1, 2, and 3 During Murine Development," <i>Develop. Dynamics</i> 197:40-56 (1993)
	AT	<u>4</u>	Iruela-Arispe, M.L. and H.F. Dvorak, "Angiogenesis: a Dynamic Balance of Stimulators and Inhibitors," <i>Thrombosis & Haemostasis</i> 78:672-677 (July 1997)

EXAMINER

DATE CONSIDERED

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APPLICANT Iruela-Arispe <i>et al.</i>		
FILING DATE August 13, 1999		GROUP To be assigned

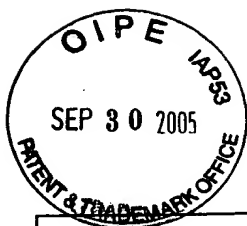
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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	5	Kuno, K. <i>et al.</i> , "Molecular Cloning of a Gene Encoding a New Type of Metalloproteinase-disintegrin Family Protein with Thrombospondin Motifs as an Inflammation Associated Gene," <i>J. Biol. Chem.</i> 272:556-562 (January 1997)
	AS	5	Kyriakides, T.R. <i>et al.</i> , "Mice That Lack Thrombospondin 2 Display Connective Tissue Abnormalities That Are Associated with Disordered Collagen Fibrillogenesis, an Increased Vascular Density, and a Bleeding Diathesis," <i>J. Cell Biol.</i> 140:419-430 (January 1998)
	AT	5	Lawler, J. <i>et al.</i> , "Thrombospondin-1 Is Required for Normal Murine Pulmonary Homeostasis and Its Absence Causes Pneumonia," <i>J. Clin. Invest.</i> 101:982-992 (March 1998)

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>6</u>	Nishimori, H. <i>et al.</i> , "A novel brain-specific p53-target gene, BAI1, containing thrombospondin type 1 repeats inhibits experimental angiogenesis," <i>Oncogene</i> 15:2145-2150 (October 1997)
	AS	<u>6</u>	Pfaff, M. <i>et al.</i> , "Comparison of Disintegrins with Limited Variation in the RGD Loop in Their Binding to Purified Integrins α IIb β 3, α V β 3 and α 5 β 1 and in Cell Adhesion Inhibition," <i>Cell Adhesion & Comm.</i> 2:491-501 (1994)
	AT	<u>6</u>	Rawlings, N.D. and A.J. Barrett, "Evolutionary Families of Metallopeptidases," <i>Meth. Enzymol.</i> 248:183-229 (1995)

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	Z	Tolsma, S.S. <i>et al.</i> , "Peptides Derived from Two Separate Domains of the Matrix Protein Thrombospondin-1 Have Anti-Angiogenic Activity," <i>J. Cell Biol.</i> 122:497-511 (1993)
	AS	Z	Usami, Y. <i>et al.</i> , "A 28 kDa-protein with disintegrin-like structure (jararhagin-C) purified from <i>Bothrops jararaca</i> venom inhibits collagen- and ADP-induced platelet aggregation," <i>Biochem. & Biophys. Res. Comm.</i> 201:331-339 (1994)
	AT	Z	Vogel, T. <i>et al.</i> , "Modulation of Endothelial Cell Proliferation, Adhesion, and Motility by Recombinant Heparin-Binding Domain and Synthetic Peptides From the Type I Repeats of Thrombospondin," <i>J. Cell. Biochem.</i> 53:74-84 (1993)

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>8</u>	Wolfsberg, T.G. and J.M. White, "Review: ADAMS in Fertilization and Development," <i>Develop. Biol.</i> 180:389-401 (1996)
	AS	<u>8</u>	GenBank Accession No. D67076, Kuno, K. (February 1999)
	AT	<u>8</u>	GenBank Accession No. AB001735, Kuno, K. (January 1998)

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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	2	GenBank Accession No. X14787, Hennessy, S.W. <i>et al.</i> (1995)
	AS	2	GenBank Accession No. U64857, Wilson, R. <i>et al.</i> (November 1998)
	AT	2	GenBank Accession No. X04665, Lawler, J. and R.O. Hynes (1995)

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	AO						Yes No
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>10</u>	GenBank Accession No. M64866, Bornstein, P. <i>et al.</i> (1993)
	AS	<u>10</u>	GenBank Accession No. L07803, Laherty, C.D. <i>et al.</i> (1994)
	AT	<u>10</u>	GenBank Accession No. U08006, Michelotti, G.A. <i>et al.</i> (1995)

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	AR	<u>11</u>	GenBank Accession No. M16974, Rao, A.G. <i>et al.</i> (1994)
	AS	<u>11</u>	GenBank Accession No. L13855, Dean, H.J. and A.K. Cheung (1994)
	AT	<u>11</u>	GenBank Accession No. AL021529, Murphy, L. and D. Harris (January 1998)

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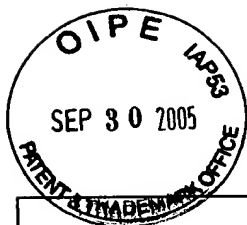
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	AR	<u>12</u>	GenBank Accession No. D86074, Sudo, S. (February 1999)
	AS	<u>12</u>	GenBank Accession No. L05390, Blanco, G. <i>et al.</i> (1993)
	AT	<u>12</u>	GenBank Accession No. Z69361, Gajadsty, S. <i>et al.</i> (November 1998)

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	AR	<u>13</u>	GenBank Accession No. X99599, Borghese, R. <i>et al.</i> (February 1998)
	AS	<u>13</u>	GenBank Accession No. AF018073, Schneider, K.H. <i>et al.</i> (October 1997)
	AT	<u>13</u>	GenBank Accession No. L23760, Lin, Q. <i>et al.</i> (1994)

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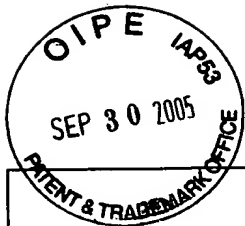
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	AR	<u>14</u>	GenBank Accession No. Z46970, Wiese, M. (1995)
	AS	<u>14</u>	GenBank Accession No. AC004449, Lamerdin, J.E. <i>et al.</i> (September 1998)
	AT	<u>14</u>	GenBank Accession No. Z69589, Dreusch, A. <i>et al.</i> (1996)

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	AR	<u>15</u>	GenBank Accession No. Z22279, Zabarovsky, E. <i>et al.</i> (1994)
	AS	<u>15</u>	GenBank Accession No. X17524, Ohama, T. <i>et al.</i> (1992)
	AT	<u>15</u>	GenBank Accession No. AB005287, Ueno, A. <i>et al.</i> (March 1998)

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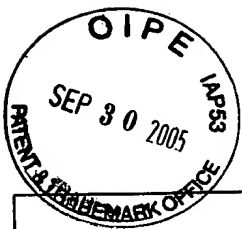
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	AR	<u>16</u>	GenBank Accession No. X87619, Zafar, R.S. (1995)
	AS	<u>16</u>	GenBank Accession No. M87276, Laherty, C.D. <i>et al.</i> (1994)
	AT	<u>16</u>	GenBank Accession No. M62458, Lawler, J. <i>et al.</i> (1994)

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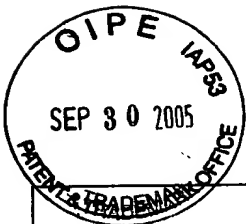
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	AR	<u>17</u>	GenBank Accession No. AB002364, Nagase, T. <i>et al.</i> (February 1999)
	AS	<u>17</u>	GenBank Accession No. AB005297, Nakamura, Y. <i>et al.</i> (November 1997)
	AT	<u>17</u>	GenBank Accession No. X69161, Akam, M.E. <i>et al.</i> (1995)

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	AR	<u>18</u>	GenBank Accession No. X16619, Debuchy, R. <i>et al.</i> (February 1999)
	AS	<u>18</u>	GenBank Accession No. 136448, Goodearl, A. <i>et al.</i> (March 1997)
	AT	<u>18</u>	GenBank Accession No. L12260, Marchionni, M.A. <i>et al.</i> (September 1997)

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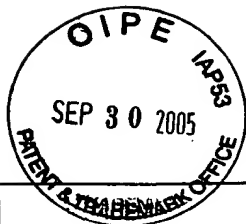
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	AR	<u>19</u>	GenBank Accession No. I36352, Goodearl, A. <i>et al.</i> (March 1997)
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	AT	<u>19</u>	GenBank Accession No. 107789, Liberator, P.A. <i>et al.</i> (1994)

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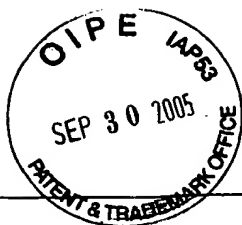
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	AR	<u>20</u>	GenBank Accession No. I08144, Altenburger, W. <i>et al.</i> (1994)
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	AT	<u>20</u>	GenBank Accession No. AF001444, Mundlos, S. <i>et al.</i> (August 1997)

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FORM PTO-1449

INFORMATION DISCLOSURE STATEMENTATTY. DOCKET NO.
1488.1070006APPLICATION NO.
09/373,658APPLICANT
Iruela-Arispe *et al.*FILING DATE
August 13, 1999GROUP
To be assigned

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
	AB						
	AC						
	AD						
	AE						
	AF						
	AG						
	AH						
	AI						
	AJ						
	AK						

FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>21</u>	English language translation of WO 98/55643 (Document AM1)
	AS		
	AT		

EXAMINER

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.



Exhibit D

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

IRUELA-ARISPE *et al.*

Appl. No. 09/373,658

Filed: August 13, 1999

For: **Meth1 and Meth2 Polynucleotides
and Polypeptides**

Art Unit: 1646

Examiner: To be assigned

Atty. Docket: 1488.1070006/EKS/AJK

First Supplemental Information Disclosure Statement

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 is a document that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of the document is submitted herewith. The numbering on this First Supplemental Information Disclosure Statement is a continuation of the numbering in Applicants' Information Disclosure Statement filed on September 16, 1999 in connection with the above-captioned application.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed a publication date on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication date should not be construed as an admission that the information was actually published on the date indicated.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior



- 2 -

IRUELA-ARISPE *et al.*
Appl. No. 09/373,658

art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that was cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This First Supplemental Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

Consideration of the cited document and making the same of record in the prosecution of the above-identified application is respectfully requested. The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036. A duplicate copy of this pleading is enclosed.

Respectfully submitted,

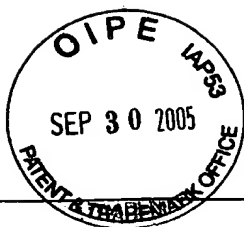
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Andrea Jo Kamage

Andrea Jo Kamage
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Date: May 10, 2000

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FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.
1488.1070006APPLICATION NO.
09/373,658APPLICANT
Iruela-Arispe *et al.*FILING DATE
August 13, 1999GROUP
1646

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA						
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FOREIGN PATENT DOCUMENTS

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	AL						Yes No
	AM						Yes No
	AN						Yes sNo
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR		
	AS	21	Vazquez, F. <i>et al.</i> , "Meth-1 and Meth-2 are Novel Proteins that Contain the Anti-Angiogenic Domain of Thrombospondin 1," <i>FASEB J.</i> 11:A336, Abstract No. 1947 (February 1997)
	AT		

EXAMINER

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